Remarks/Arguments

Claims 1-17 and 20-23 are pending in the application. Claims 1-13 and 20-22 have been withdrawn from consideration pursuant to a lack of unity objection. Claims 14-17 and 23 are under consideration.

The Examiner has rejected claims 14-17 and 23 under 35 U.S.C. §112, 1st paragraph, alleging a lack of written description. The Examiner states that the claimed genus is an "immunogenic determinant or cell residue," and that this genus is highly variant. The Examiner alleges that the specification and claims do not indicate the distinguishing attributes shared by the members of this genus. Applicant respectfully disagrees.

Claims 14 and 15 have been amended to more particularly point out and define the invention. The claimed genus is not an "immunogenic determinant or cell residue" as alleged by the Examiner. Rather, the claimed genus is a vaccine composition comprising *a prokaryotic cell or cell residue of a prokaryotic cell*, wherein the prokaryotic cell has an increased concentration of trehalose. The amendments to claim 14 and 15 clarify this relationship.

The specification provides sufficient written description for the claimed genus of a prokaryotic cell or cell residue of a prokaryotic cell. The specification clearly defines "prokaryotic cell" (p. 4, line 30-p. 5, line 2). This definition provides many structural attributes that are common elements of the claimed genus of prokaryotic cells and which distinguish prokaryotic cells from non-prokaryotic cells. As indicated in the specification, prokaryotic cells are unicellular organisms, lack organelles such as mitochondria, chloroplasts and Golgi apparatus, lack a discrete cytoskeleton and lack a discrete nucleus. The specification also discloses examples of prokaryotic cells useful in the invention: bacteria, archaebacteria, rickettsias, mycoplasmas, spiroplasmas and chlamydiae (p. 5, lines 2-7). In addition, numerous examples of specific bacteria that may be used in the inventive composition are taught in the specification, including, but not limited to, Enterobacteriaceae, halophilic and halotolerant bacteria, micro-coccocaceae, Rhizobium species, Cyanobacteria, and Mycobacteria (p. 5, lines 2-24). Examples 4 and 5 are working examples that utilize E. coli and Salmonella typhimurium in embodiments of the inventive composition. Furthermore, at the time the application was filed,

prokaryotic cells were well known in the art. Thus, as summarized in MPEP 2163 II(A)(3), there is no need to disclose in detail what is conventional or well known to one of ordinary skill in the art. Consequently, the skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing.

Examiner alleges that to satisfy adequate written description, "the protein itself is required" and that "the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling with the scope of the claimed genus." The operative element of claim 14 or 15 is a prokaryotic cell or cell residue of a prokaryotic cell, not a protein or a DNA molecule. Thus, a recitation of a protein or DNA is not required for adequate written description of the claimed invention.

Applicant respectfully requests reconsideration and withdrawal of the Section 112 rejection.

Response to Section 102 Rejection

Claims 14-17 and 23 have been rejected as being anticipated by Tunnicliffe et al. WO 98/24882 or Tunnacliffe et al. US 6,468,782 (collectively, "Tunnacliffe").

Tunnacliffe deals with using trehalose to stabilize cells. One of the uses of the drying/stabilization method cited in Tunnacliffe is for dying cells which may have utility in vaccines. In such a use, the method of Tunnacliffe provides for cells of a whole-cell live attenuate vaccine to be dried for long term storage. Following storage, the cells can be rehydrated.

The teachings of Tunnacliffe in relation to the utility of the disclosed stabilization method as applied to vaccine compositions is thus restricted solely to cell storage. The Tunnacliffe invention was based on the finding that trehalose had a structure very similar to water. The inventors of the Tunnacliffe patent, which include the inventor of the instant application, identified that the presence of trehalose within a cell during drying would result in the maintenance of the structure as the cell was dried. This maintenance of structure results in the cell being maintained in an intact state (i.e. having a structure as if water was still present within

the cell). Hence, trehalose effectively replaces the water content in dried out cells and due to its structure keeps the cell in the same "shape" that it would have been had it been fully hydrated.

There is no suggestion that the teaching of Tunnacliffe could be extended to improving an immune response using cells dried in trehalose. Most importantly, at no time did Tunnacliffe or any of the other inventors recognize that inducing trehalose within the cell would make a cell more immunogenic.

Further, as Tunnacliffe was concerned only with the drying of cells in a stable manner, there was only consideration of a two-step drying process which comprises the steps of (1) inducing trehalose within a cell and (2) further drying the cell with carbohydrate about the outside of the cell (a stabilizing agent).

According to the present invention, bacterial cells in which trehalose is induced become more immunogenic. The cells do not have to be dried to achieve this objective. Step 2 of Tunnacliffe, drying of the cell with carbohydrate, need not be performed. Tunnacliffe discloses only that the cells prepared according to the methods described therein could be used for live bacterial vaccines *in a dry stable form* (see column 4, line 32). Accordingly, the skilled artisan would not look to Tunnacliffe for guidance on the preparation of live bacterial vaccines which were in a form *other than* a dry, stabilized form.

According to claims 14 and 15, a vaccine composition comprises a prokaryotic cell or cell residue of a prokaryotic cell, which cell has been treated to increase the concentration of trehalose therein *without subsequent drying of the cell in the presence of a non-reducing carbohydrate*. As indicated in response to the previous office action, Tunnacliffe does not disclose a vaccine composition comprises a prokaryotic cell or cell residue of a prokaryotic cell, which cell has been treated to increase the concentration of trehalose therein *without subsequent drying of the cell in the presence of a non-reducing carbohydrate*.

Examiner now alleges that Tunnacliffe Example 7 teaches a composition identical to applicant's claimed composition. Applicant respectfully points out the following. First, there is no suggestion, teaching or acknowledgement in the Tunnacliffe document that the cells treated according to the described method are more immunogenic as a result of the intracellular induction of trehalose. Second, Example 7 is a protocol used only to quantify the amount of

trehalose in the cells of Tunnacliffe. There is no suggestion that these intermediate stage cells would actually have utility as a vaccine. They would not be used as a vaccine in the intermediate form disclosed in Example 7. Also, they would not be suited for storage according to the teachings of Tunnacliffe since they have not been dried. In this light, the intermediate form composition of Example 7 is not a "vaccine composition" within the meaning of claims 14 and 15, and does not anticipate those claims.

Furthermore, the Example 7 preparation does not contain an adjuvant, and therefore does not anticipate claim 16. Moreover, since the material would not be viewed as a vaccine composition, there would have been no incentive to modify it to add an adjuvant. Claim 16 is therefore not rendered obvious over Tunnacliffe.

Reconsideration and withdrawal of the Section 102 rejection of claims 14-17 and 23 is respectfully submitted.

The claims of the application are believed in condition for allowance. An early action toward that end is earnest solicited.

Respectfully submitted
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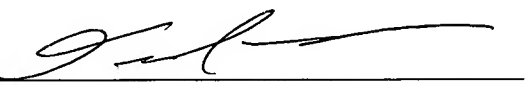
BY 

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